REMARKS

It appears from the Examiner's search strategy (copy enclosed) and cited references that the Examiner has conducted a search and examination beyond the scope of the elected Group I, *i.e.*, the NOI. This is very much appreciated and underscores the difficulty of performing a search of an aspect of the invention that is not the invention *per se*. Therefore, it seems unnecessary that Applicants should have to file divisional applications on the basis of Groups II and III when the conducted search and cited art clearly indicate that a search of the invention, *i.e.*, RabiesG pseudotyped lentiviral-mediated gene therapy for treating motor neuron disease, is sufficient to find all of the relevant art that would generally apply to the claimed subject matter. Accordingly, Applicants request withdrawal of the restriction requirement on the basis of the conducted search and examination.

The Examiner is thanked for his helpful remarks in the Office Action.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-9, 32-36, 45 and 46 are pending in this application. Claims 10-31, 37-44 and 47-50 are cancelled in an effort to advance prosecution. Applicants expressly reserve the right to pursue the cancelled subject matter in a continuing application. No new matter is added.

It is submitted that the claims are patentably distinct over the prior art and that these claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the amendments should not give rise to any estoppel, as they are not narrowing amendments.

Priority

Certified copies of application nos. UK 0223076.1, UK 0228314.1 and UK 0318213.6 have been requested and will be filed upon receipt by the undersigned.

II. THE REJECTIONS UNDER 35 U.S.C. § 112, 1ST PARAGRAPH, ARE OVERCOME

Claims 1, 10, 11 and 20 were rejected under the first paragraph of Section 112 as allegedly lacking adequate written description. The rejection is traversed.

The Office Action asserted that the genus of mutants, variants, homologues and fragments of rabies G protein was not possessed by the inventors. Claims 10, 11 and 20 have been cancelled, rendering the rejection with respect to those claims moot.

Claim 1 recites "a rabies G envelope protein." As used in the specification (see page 7, lines 1-2, 11-12, 16-17 and 22-23; page 33, line 25; and page 34, line 5), the term "rabies G envelope protein" is followed by the phrase "or a mutant, variant, homologue or fragment thereof," (emphasis added) indicating that the term "rabies G envelope protein" does not itself include mutants, variants, homologues or fragments. It is conceded that cancelled claims 10 and 20 were improperly dependent in that they expanded the scope of the independent claims from which they depended.

Rabies G proteins are known in the art and described in the application beginning at page 34, line 10. Accordingly, claim 1 is adequately described. Reconsideration and withdrawal of the written description rejection are requested.

Claims 1-34, 36-38, 40-42 and 44 were rejected under the first paragraph of Section 112 as allegedly lacking enablement. The rejection is traversed.

The Examiner asserts that the claims are not enabled for lentiviral-mediated gene therapy of motor neuron disease. Applicants disagree. The claims are enabled for their full scope, directed to Rabies-G pseudotyped lentiviral-mediated gene therapy of motor neuron disease.

The claims are limited to treating motor neuron disease. The Examiner erroneously grouped Parkinson's disease ("PD") with motor neuron disease. While both PD and motor neuron diseases, such as amyotrophic lateral sclerosis ("ALS") and spinal muscular atrophy ("SMA"), are neurodegenerative, PD is not a motor neuron disease. Motor neurons are the neurons that activate muscle cells. Therefore, the claims do not read on the treatment of PD and the Examiner's reference to the use of GDNF for treating Parkinson's disease is off-point.

Moreover, gene therapy is quite different than the protein therapy to which the Examiner refers. This point is underscored by the positive data resulting from lentiviral-mediated delivery of GDNF in non-human primate models of PD. Palfi *et al.*, Journal of Neuroscience, 2002, 22(12): 4942-54. (Copy enclosed.) Regardless, as mentioned above, lentiviral-mediated gene therapy of PD is not within the scope of the claimed invention.

The specification describes the claimed invention directed to Rabies G pseudotyped lentiviral-mediated gene therapy of motor neuron disease. Following the guidelines set forth in

the specification, Applicants have developed several preclinical products for the treatment of motor neuron disease. For example, Applicants have reported therapeutic results in art-recognized mice models for ALS and SMA.

In an art-recognized mouse model for ALS, transgenic mice with a SOD-1 (superoxide dismutase) mutation typically survive an average of 125-130 days, and die from diaphragm muscle failure, as is the case with ALS patients. Following the teachings of the specification (*e.g.*, Example 17), Applicants administered a rabies G pseudotyped lentiviral vector carrying the neuroprotective gene, VEGF, via the diaphragm muscle to target diaphragm motor neurons. As a result, Applicants were able to significantly prolong the survival of the treated SOD-1 mutant mice, as compared to untreated mutant mice. Azzouz *et al.*, Nature, 2004, 429: 413-17. (Copy enclosed.)

In an art-recognized mouse model for SMA, transgenic mice lacking the gene for SMN (survival motor neuron), and transformed with human SMN2, represent an animal model of type 1 (severe) SMA. The mice die at approximately 13 days of age; muscular atrophy is due to degeneration of motor neurons in the spinal cord. Following the guidelines of the specification (*e.g.*, Example 16), Applicants administered, via the major muscle groups of the mice, a rabies G pseudotyped lentiviral vector carrying the SMN gene. The motor neurons projecting into the muscle were transduced, and as a result, prolonged survival of the treated mice as compared to untreated transgenic mice was observed. Azzouz *et al.*, J. Clin. Invest., 2004, 114: 1726-31. (Copy enclosed.)

As further proof of principle, following the guidelines of the specification, Applicants have carried out and reported other therapeutic work in art-recognized models for ALS using Rabies-G pseudotyped lentiviral vectors targeting motor neurons. These vectors carry NOIs encoding GDNF, IGF-1, and RNAi, which silences the SOD-1 mutation in mice receiving the vector. Guillot *et al.*, Neurobiol. Disease, 2004, 16(1): 139-149; Teng *et al.*, Neurobiol. Disease, 2005, 20: 694-700; and Ralph *et al.*, Nat. Med., 2005, 11(4): 429-33. (Copies enclosed.)

Accordingly, the specification enables the claimed invention. Reconsideration and withdrawal of the enablement rejection are requested.

III. THE REJECTIONS UNDER 35 U.S.C. § 102 ARE OVERCOME

Claims 11, 20 and 21 were rejected under Section 102(a) as allegedly being anticipated by Reiser *et al.* These claims have been cancelled, obviating the rejection.

Claims 1-5, 7, 8, 10-14, 17, 18, 20-24, 27, 28, 30, 32, 34, 38 and 42 were rejected under Section 102(e) as allegedly being anticipated by Mitrophanous *et al.* This reference is not by "another," as required by Section 102(e). Mitrophanous *et al.* and the instant application share common inventors and are commonly assigned. (Assignment of the present application is set out at reel 018233, frame 0552.) The disclosure of Mitrophanous *et al.* does not qualify as prior art under Section 102(e) because it was not known or used by others "before the invention thereof by the applicant for patent." 35 U.S.C. §102(e). Because of the overlap in inventorship between the cited document and the instant application, the content of the cited document could not have been known or used by others "before the invention thereof by the applicant for patent." In light of the foregoing, Applicants submit that no *prima facie* case of anticipation is present and this rejection may properly be withdrawn.

Claims 1-5, 7, 8, 10-14, 17, 18, 20-24, 27, 28, 30, 32, 34, 38 and 42 were rejected under Section 102(f) because the Applicant allegedly did not invent the claimed subject matter. As discussed above, Mitrophanous *et al.* and the present invention are commonly owned and have overlapping inventorship. Moreover, the scope of the claims in Mitrophanous *et al.* is not identical with the scope of the present claims, thereby explaining the difference in inventorship.

Claims 1-5, 7-15, 27-32, 34, 36, 38, 40, 42 and 44 were rejected under Section 102(f) because the Applicant allegedly did not invent the claimed subject matter. The inventors of U.S. 2004/0266715 are not "another" with respect to the present inventors, and the applications are commonly assigned. Moreover, the claimed invention of this co-pending application is distinct from the instant invention in that the subject matter of 2004/0266715 is directed to RARβ2-gene therapy of injured neurons by the promotion of the growth of injured nervous tissue. Injured nervous tissue is the result of spinal injury, peripheral injury or avulsion. These indications are distinct from motor neuron disease, which is due to pathological degeneration of neurons. Different, but overlapping, inventorship is completely consistent with the distinct claim scope between 2004/0266715 and the present application.

Reconsideration and withdrawal of the art rejections are requested.

IV. THE DOUBLE PATENTING REJECTION IS OVERCOME

Claims 1-4, 7, 8, 10-14, 17, 18, 20-24, 27, 28, 30, 32, 34, 38 and 42 were provisionally rejected on the ground of non-statutory obviousness-type double patenting. The rejection is traversed.

Contrary to the statement at page 16 of the Office Action, the claims of U.S.S.N. 10/838,906 are not species of the present claims. The present claims are directed to rabies-G lentiviral-mediated gene therapy of motor neuron disease. The co-pending claims of U.S.S.N. 10/838,906 are directed to RARβ2-gene therapy of injured nervous tissue by promotion of nervous tissue growth. Motor neuron disease, the treatment of which is claimed in the instant application, is distinct from neuronal trauma, such as spinal injury, peripheral injury or avulsion, as described in the co-pending application. Therefore, reconsideration and withdrawal of the provisional double patenting rejection are requested.

CONCLUSION

Applicants believe that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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